

IN THE CLAIMS:

Claim 1 (withdrawn): A method of modulating cell proliferation comprising contacting a cell with a composition comprising a variant type 2 methionine aminopeptidase ("MetAP2"), which has dominant negative MetAP2 activity and comprises a translation domain.

Claim 2 (withdrawn): The method of claim 1 wherein the cell is an endothelial cell.

Claim 3 (withdrawn): The method of claim 2 wherein the endothelial cell is in vitro.

Claim 4 (withdrawn): The method of claim 1 wherein the composition consists essentially of a variant MetAP2 translation domain.

Claim 5 (withdrawn): The method of claim 4 wherein the translation domain consists of a sequence identified by SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 or SEQ ID NO:15.

Claim 6 (withdrawn): The method of claim 1 wherein the composition consists of an amino acid sequence identified by SEQ ID NO:6 and wherein the amino acid at position 231 of SEQ ID NO:6 is Alanine.

Claim 7 (withdrawn): The method of claim 6, wherein the composition has a sequence identified by SEQ ID NO:6, 7, 8, or 16.

Claim 8 (withdrawn): The method of claim 1 wherein the translation domain has a sequence identified by SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 or SEQ ID NO:15.

Claim 9 (presently amended): A method of decreasing ~~modulating~~ cell proliferation, the method comprising contacting a eukaryotic cell comprising a wild-type MetAP2 with a composition comprising an isolated ~~and purified~~ polynucleotide, wherein the polynucleotide encodes a variant eukaryotic MetAP2 that lacks aminopeptidase activity, comprises a eukaryotic translation domain, and possesses dominant negative MetAP2 activity ~~has dominant negative methionine MetAP2 activity and comprises a translation domain, such that the dominant negative activity of the variant MetAP2 decreases the proliferation of the cell.~~

Claim 10 (presently amended): The method of claim 9, wherein the cell is an endothelial cell.

Claim 11 (presently amended): The method of claim 9, wherein the polynucleotide is part of a vector and is operably linked to a promoter.

Claim 12 (presently amended): The method of claim 11, wherein ~~said~~ the vector is an adenovirus vector.

Claim 13 (presently amended): The method of claim 11, wherein ~~said~~ the promoter is a CMV promoter.

Claim 14 (presently amended): The method of claim 11, wherein ~~said~~ the vector is an adenovirus vector and ~~said~~ the promoter is a CMV promoter.

Claim 15 (presently amended): The method of claim 9, wherein the variant MetAP2 consists essentially of a an amino acid sequence selected from the group of amino acid sequences consisting of ~~identified by~~ SEQ ID NO:6, 7, 8, ~~or~~ and 16.

Claim 16 (presently amended): The method of claim 9₁ wherein the variant MetAP2 consists essentially of a eukaryotic translation domain.

Claim 17 (presently amended): The method of claim 16₁ wherein the translation domain is selected from the group of sequences consisting of ~~has a sequence identified by~~ SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 ~~or~~ and SEQ ID NO:15.

Claim 18 (presently amended): The method of claim 9₁ wherein the polynucleotide has a sequence selected from the group of sequences consisting of ~~identified in any one of~~ SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:18.

Claim 19 (withdrawn): A method of modulating cell proliferation comprising contacting a cell with a composition consisting essentially of a variant type 2 methionine aminopeptidase (MetAP2) translation domain that has dominant negative MetAP2 activity.

Claim 20 (withdrawn): The method of claim 19 wherein said composition consists of a variant MetAP2 translation domain that has dominant negative MetAP2 activity.

Claim 21 (new): The method of claim 9, wherein the variant MetAP2 comprises a eukaryotic translation domain and lacks a functional active site pocket such that the variant MetAP2 lacks aminopeptidase activity and possesses dominant negative MetAP2 activity.

Claim 22 (new): The method of claim 9, wherein the variant MetAP2 comprises a eukaryotic translation domain and lacks the ability to bind fumagillin, such that the variant MetAP2 lacks aminopeptidase activity and possesses dominant negative MetAP2 activity.

Claim 23 (new): The method of claim 22, wherein the variant MetAP2 lacks the ability to bind fumagillin because the conserved histidine has been replaced with an amino acid other than histidine.

Claim 24 (new): The method of claim 9, wherein the variant MetAP2 comprises a eukaryotic translation domain and lacks the ability to coordinate a cobalt ion such that the variant MetAP2 lacks aminopeptidase activity and possesses dominant negative MetAP2 activity.

Claim 25 (new): A method of decreasing cell proliferation, the method comprising contacting a mammalian cell comprising a wild-type MetAP2 with a composition comprising an isolated polynucleotide, wherein the polynucleotide encodes a variant mammalian MetAP2 that lacks aminopeptidase activity, comprises a mammalian translation domain, and possesses dominant negative MetAP2 activity, such that the variant MetAP2 decreases the proliferation of the cell.

Claim 26 (new): The method of claim 25, wherein the cell is an endothelial cell.

Claim 27 (new): The method of claim 25, wherein the polynucleotide is part of a vector and is operably linked to a promoter.

Claim 28 (new): The method of claim 25, wherein the mammalian cell is a human cell.

Claim 29 (new): The method of claim 25, wherein the variant MetAP2 comprises a mammalian translation domain and lacks a functional active site pocket such that the variant MetAP2 lacks aminopeptidase activity and possesses dominant negative MetAP2 activity.

Claim 30 (new): The method of claim 29, wherein the amino acid sequence of the mammalian translation domain is selected from the group of amino acid sequences consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:15.

Claim 31 (new): The method of claim 25, wherein the variant MetAP2 comprises a mammalian translation domain and lacks the ability to bind fumagillin, such that the variant MetAP2 lacks aminopeptidase activity and possesses dominant negative MetAP2 activity.

Claim 32 (new): The method of claim 31, wherein the variant MetAP2 lacks the ability to bind fumagillin because the conserved histidine has been mutated to an amino acid other than histidine.

Claim 33 (new): The method of claim 32, wherein the amino acid sequence of the variant MetAP2 is selected from the group of amino acid sequences consisting of SEQ ID NO: 6, SEQ ID NO:7, SEQ ID NO: 8 and SEQ ID NO:16.

Claim 34 (new): The method of claim 31, wherein the amino acid sequence of the mammalian translation domain is selected from the group of amino acid sequences consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:15.

Claim 35 (new): The method of claim 25, wherein the variant MetAP2 comprises a eukaryotic translation domain and lacks the ability to coordinate a cobalt ion such that the variant MetAP2 lacks aminopeptidase activity and possesses dominant negative MetAP2 activity.

Claim 36 (new): The method of claim 35, wherein the amino acid sequence of the mammalian translation domain is selected from the group of amino acid

sequences consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:15.

Claim 37 (new): A method of decreasing cell proliferation, the method comprising contacting a yeast cell comprising a wild-type MetAP2 with a composition comprising an isolated polynucleotide, wherein the polynucleotide encodes a variant yeast MetAP2 that has the amino acid sequence of SEQ ID NO: 8 and possesses dominant negative MetAP2 activity, such that the variant MetAP2 decreases the proliferation of the cell.

Claim 38 (new): The method of claim 35, wherein the polynucleotide comprises the nucleic acid sequence of SEQ ID NO:11.